IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Art Unit: 1632
	)	
OKURA et al.	)	Examiner: R. Shukla
	)	
Appln. No.: 09/479,862	)	Washington, D.C.
	)	
Filed: January 1, 2000	)	January 15, 2003
	)	
For: GENOMIC DNA ENCODING A POLYPEPTIDE CAPABLE OF...	)	Atty. Docket: OKURA=1A
	)	
Confirmation No.: 3626	)	

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REPLY

Honorable Commissioner for Patents
Washington, D.C. 20231

Sir:

In the Advisory Action dated December 20, 2002, the examiner indicated that no new evidence had been presented to obviate the rejections of record and therefore, the §112, first paragraph, enablement rejection was maintained.

Attached hereto is a copy of Goto et al., "Construction and Analysis of New Vector Systems with Improved Interleukin-18 Secretion in a Xenogeneic Human Tumor Model", J. Immunotherapy 25 (Suppl. 1):535-541 (2002), as new evidence that the presently claimed invention is enabled. As demonstrated in the results presented (i.e., Fig. 4) and discussed on page 539, right column, that:

> Intraperitoneal injection of the IL-18 adenoviral vector (Ad.IL-Ira.IL-18) inhibited the development of intraperitoneal dissemination of tumor and was associated with elevation of serum IL-18 and IFN-γ levels.

Goto et al. further disclosed on page S40, left column, that:

> Intraperitoneal injection of an IL-18 adenoviral vector (Ad.IL-1ra.IL-18) inhibited

> tumor establishment *in vivo* (Fig. 4). We studied which organs in the peritoneal cavity mainly express the transduced gene using an adenoviral vector expressing the β-galactosidase gene as a marker. The tumor, the liver, the intestine, and the mesenterium are primarily stained blue (Goto et al., unpublished data). We believe that those organs as well as tumor are the source of IL-18 production when Ad.IL-1ra.IL-18 is administrated i.p.

and on page S40, right column, that:

> In conclusion, we demonstrated significant antitumor effects of an IL-18 adenoviral vector, which is capable of efficiently producing bioactive IL-18. Intraperitoneal injection of Ad.IL-1ra.IL-18 successfully managed peritoneal carcinomatosis concomitant with augmented antitumor effects of peritoneal macrophages. These results indicate that our new vector systems using IL-1ra leader sequence may be useful in clinical application of IL-18 gene therapy.

Accordingly, based on the guidance provided in the present specification, the presently claimed invention is enabled to one of skill in the art.

Reconsideration and withdrawal of the enablement rejection are therefore respectfully requested.

In view of the above, the present claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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